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ELLIS, J EXAMINER

18N1/0401

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ART UNIT	PAPER NUMBER
1813	11

DATE MAILED: 04/01/94

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☐ This application has been examined ☒ Responsive to communication filed on 12/17/93 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-4 and 6-21 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 5 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-4 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

Applicant's election with traverse of Group I, claims 1-5 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the Examiner has failed to provide an explanation as to how the separate classification of the groups creates a burden [on the Examiner]. This is not found persuasive because as evidenced by their separate classifications, the subject matter of each of the inventions is separate and distinct. The issues raised and the art searched for each invention type is different and, accordingly, places an undue burden on the Examiner to search and fully address all the issues.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6-21 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 10.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

As set forth in the previous office action, the specification is replete with grammatical errors too numerous to mention specifically. It is noted that applicant corrected many typographical errors in the amendment submitted in Paper No. 10; however, further revision of the specification is necessary. Examples of such errors are: on p. 55, line 9, "proliferation" is misspelled, on p. line 22, "activation" is misspelled, on p. 58, line 16, "similar" is misspelled, *etc.*.

Claims 1-4 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility.

The claims are rejected for the reasons set forth on pp. 4-6 of the previous office action.

Applicant argues that (i) 4-1BB is an inducible receptor-like protein expressed in different cell types, (ii) cross-linking 4-1BB with the monoclonal antibody 53A2 resulted in enhancement of T cell proliferation, and (iii) that the addition of paraformaldehyde-fixed SF21 cells expressing recombinant 4-1BB, synergized with f(ab'), anti-mu in inducing splenic B-cell proliferation. These arguments have been considered, but are not persuasive for several reasons. First, the descriptive characteristics disclosed in the specification are the initial experimental steps performed in order to ascertain what is the actual biological role and/or use of 4-1BB. These characteristics do not disclose (i) the biological activity of 4-1BB, or (ii) how to use 4-1BB. Second, the expression of 4-1BB in different cell types does not provide a patentable utility for the protein because this characteristic does not disclose its function or how to use the protein. The cross-linking of 4-1BB with a monoclonal antibody is not evidence of the actual activity of 4-1BB. The specification teaches that these data merely *suggest* that 4-1BB has the *potential* to function as an accessory signaling molecule during T cell activation and proliferation. See p. 56, lines 22-25. The specification discloses that the experiments involving the paraformaldehyde-fixed SF21 cells expressing recombinant 4-1BB which synergized with f(ab'), anti-mu to induce splenic B-cell proliferation merely *suggest* that 4-1BB *may* act as a regulator of B-cell growth. See p. 67, lines 24-28. Accordingly, the specification is merely

speculating as to possible roles of 4-1BB, but fails to disclose how one skilled in the art can use the claimed invention.

Applicant urges that the holding in Brenner v. Manson, 383 U.S. 519, 148 U.S.P.Q. 689 (1966) merely requires the demonstration of a practical utility and not a utility with commercial value. Further, that the instant protein acts as a signaling molecule and that this activity is inherently useful. These arguments have been considered, but are not persuasive. The Supreme Court held in Brenner v. Manson, *supra*, that the utility of an invention must be definite and in a currently available form. Products which have no known use or which are useful only as an object of scientific research are not useful within the meaning of 35 U.S.C. §101. The Court further held that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". Brenner v. Manson 148 U.S.P.Q. at 696. The specification fails to disclose a utility for 4-1BB other than as an object of further scientific research. Further, even as late as 1992, Chalupny et al. teach that the function of 4-1BB was still unknown. In addition, applicants have failed to disclose what inherent use the signal molecule has. Accordingly, this argument is merely the argument of counsel and is unsupported by evidence or declarations of those skilled in the art. Counsel's arguments can not take the place of objective evidence. See In re Langer, 503 F.2d 1380, 183 U.S.P.Q. 288 (C.C.P.A. 1974); In re Payne, 203 U.S.P.Q. 245.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling

disclosure for the reasons set forth in the previous office action.

Claim 4 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Applicant argues that (i) the specification discloses that the probes must be capable of being used to isolate "similar" sequences, (ii) the term "similar" is not vague and indefinite, (iii) DNA probes are not used in activity assays, (iv) references discussing the intercrine β-subfamily have been incorporated into the specification by reference, and (v) many modifications can be made to the instant DNA sequence without affecting the amino acid sequence. Accordingly, derivatives are contemplated within the scope of the invention. These arguments have been considered, but are not persuasive for several reasons. First, applicant's assertions that the claimed probes have been disclosed and that the term "similar" is not vague and indefinite are merely arguments of counsel and are unsupported by evidence or declarations of those skilled in the art. As set forth above, counsel's arguments can not take the place of objective evidence. See In re Langer, *supra*; In re Payne, *supra*. Further, contrary to applicant's assertion, the term "derivatives" encompasses more than silent codon changes, but also encompasses DNA sequences which encode all analogs of the instant protein. Given that the biological role of 4-1BB has not been disclosed, the specification fails to enable one skilled in the art to determine what constitutes a "similar" protein, what alterations can be made to the instant sequence that do not affect the biological activity of the protein, or which probes to employ to isolate "similar" proteins. Second, applicant appears to be arguing that the references discussing the intercrine β-subfamily constitute "essential material". "Essential material" is that which is necessary to

(i) describe the claimed invention, (ii) provide an enabling disclosure of the claimed invention, or (iii) describe the best mode (35 U.S.C. §112). An application for a patent may incorporate essential material only by reference to a U.S. patent or an allowed U.S. application in which the issue fee has been paid, and not by reference to a non-patent publication. See M.P.E.P. § 608.01(p). Accordingly, applicants reliance on the incorporation on non-patent publications is misplaced. Finally, applicant's argument with respect to DNA probes as not being useful in activity assays is unclear and, accordingly, cannot be addressed at this time.

Claim 4 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As set forth in the previous office action, claim 4 is vague and indefinite in the recitation of fragments and derivatives of the 4-1BB cDNA which can be used a probes. It is not clear which nucleotide sequences applicants intend. The claim is further vague and indefinite in the recitation of proteins which are "similar" to the 4-1BB protein. It is not clear what nucleotide/amino acid sequences applicants intend.

Applicant argues that he believes the rejection of claim 4 to be in error; however, he has not stated any reasons for his belief. Accordingly, this argument is merely the argument of counsel and is unsupported by evidence or declarations of those skilled in the art. As set forth above, counsel's arguments can not take the place of objective evidence. See In re Langer, *supra*; In re Payne, *supra*.

Claims 1-4 are rejected under 35 U.S.C. § 103 as being unpatentable over Kwon et al. Proc. Natl. Acad. Sci. USA 84:2896 (1987) in view of Maniatis et al. for the reasons set forth in the previous office action.

Applicant argues that Kwon et al. only teach the isolation of partial fragments of the instant cDNA and that none of the cDNA clones contained the full nucleotide sequence. Further, that Maniatis et al. do not provide a reasonable expectation of success that the instant sequence would be isolated. These arguments have been considered, but are not persuasive. Applicant has argued and discussed the references individually without clearly addressing the combined teachings. The references were relied on in combination and were not meant to be separately considered. The claimed invention is obvious in view of the art as a whole. That is, the teachings of Kwon et al. as to the method of constructing a cDNA library and isolating a cDNA clone encoding 4-1BB and the teachings of Maniatis et al. as to the standard methods for determining the nucleotide sequence of an isolated DNA molecule would have clearly suggested to one skilled in the art a very reasonable expectation of success in isolating the instant DNA sequence. Obviousness does not require absolute predictability, only a reasonable expectation of success. See In re O'Farrell, 7 U.S.P.Q.2d 1673.

Finally, applicant argues that the Kwon et al. reference is not enabling because the cDNA clones were not deposited and that following the procedure taught by the reference would not necessarily result in the isolation of 4-1BB. These arguments have been considered, but are not persuasive. First, the fact that the clones taught by the Kwon et al. reference were not deposited does not establish that the reference is not enabling. The criteria which render a publication as

enabling as prior art are not the same as required under 35 U.S.C. §112, first paragraph to ensure that a patent application is enabling to those skilled in the art. Second, contrary to applicant's assertion, one skilled in the art could readily follow the procedures set forth in Kwon et al. reference to construct a cDNA library and isolate the instant nucleotide sequence. Applicant has failed to provide any evidence that establishes that one skilled in the art could not follow the Materials and Method section of the reference and isolate a cDNA clone encoding 4-1BB. Accordingly, as above, this argument is merely the argument of counsel and is unsupported by evidence or declarations of those skilled in the art. Further, given the standard methods in recombinant DNA technology for determining the nucleotide sequence of a cloned gene as exemplified by the teachings of Maniatis et al., it would be obvious to one skilled in the art to determine the nucleotide sequence of the isolated clones. Obviousness does not require absolute predictability, only a reasonable expectation of success. See In re O'Farrell, *supra*.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY

ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Ellis whose telephone number is (703) 308-3990.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Ellis, Ph.D.
April 1, 1994

JOAN ELLIS
PRIMARY EXAMINER
GROUP 180